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“On a Colloid Acid, a Normal Constituent of Human Urine.” By
WILLIAM MARCET, M.D., F.R.S. Received May 28, 1864*.

IN the autumn of 1862, feeling assured that, besides the known normal crystalloid compounds found in urine, this secretion contained colloid substances, I submitted samples of the healthy secretion, after concentration, first, to the process of dialysis, and then to the action of reagents, and finally succeeded in precipitating with alcohol a colloid substance exhibiting a faintly acid or neutral reaction, and containing a small proportion of ash. For a while my endeavours to obtain a definite compound from this amorphous mass were fruitless, until, on observing that basic acetate of lead produced a precipitate in its aqueous solution, I thought of examining this precipitate, and, by decomposing it with sulphuretted hydrogen, found it to consist of an organic acid combined with lead. This new acid is possessed of the properties of a colloid substance; it may be considered as having a definite combining proportion or equivalent weight, and is undoubtedly destined to become of great importance in physiological chemistry.

After having satisfied myself of the presence of a colloid acid in urine, I tried every means to obtain as much of it as possible from a given volume of the secretion, and prepare it in the pure condition; and after having experienced many difficulties, I adopted the following method as the simplest and that yielding the most satisfactory results.

Mode of Preparation of the Colloid Acid.

Urine is mixed with animal charcoal and concentrated until reduced to about one-fourth of its original bulk. It is filtered, and a solution of caustic baryta is added until complete precipitation by this agent be effected. The fluid filtered from the baryta precipitate is dialyzed without further evapo-

* Read June 16, 1864: see Abstract, vol. xiii. p. 314.

ration, for a period of about forty hours; after which it is again concentrated, filtered, and then a solution of basic acetate of lead is added to it, which produces a precipitate: care should be taken not to use more of this solution than is necessary to obtain a complete precipitation in the fluid. The precipitate appears white, although containing a little colouring-matter; it is to be collected on a filter and washed with distilled water until the washings contain but a trace of lead. The insoluble substance on the filter is a lead-compound of the organic colloid acid; it still contains a small quantity of colouring-matter, some hydrated oxide of lead, more or less chloride of lead, and perhaps traces of sulphate of lead. In order to effect the removal of these impurities, the insoluble compound is first decomposed with sulphuretted hydrogen or sulphuric acid; if sulphuretted hydrogen is employed, the excess of this gas is afterwards expelled by boiling, or better by blowing it out with a current of air.

The acid fluid being now heated with animal charcoal and filtered, loses the whole, or nearly the whole of its colouring-matter, and apparently much of its urinous smell. Any hydrochloric acid present can be easily separated from the free organic acid by treating the colourless fluid with carbonate of silver and filtering; the dissolved silver is afterwards eliminated by means of sulphuretted hydrogen, and the excess of sulphuretted hydrogen again removed by boiling the fluid, or passing through it a current of air. The careful addition of baryta-water will precipitate any sulphuric acid present. Finally the acid is precipitated afresh with basic acetate of lead, from which it is separated by decomposing the thoroughly washed precipitate with sulphuretted hydrogen.

The object of the various operations thus described will be readily understood. By evaporating urine with animal charcoal, it is first partly discoloured; the precipitation with baryta-water throws down the phosphoric and sulphuric acids and the lime of the secretion, which would interfere with further operations, and imparts to the fluid a strongly alkaline reaction, this last condition being apparently necessary to avoid a loss of the colloid acid during the dialysis. In order to prevent decomposition, which would occur by concentrating with heat a strongly alkaline urine, the fluid is dialyzed at once for about thirty-six hours, which operation removes from it a considerable proportion of its crystalloid constituents; among these are chlorides, which it is advisable to get rid of, as much as possible, before concentration and precipitation with basic acetate of lead, because by so doing a great saving in the carbonate of silver, necessary to precipitate the remaining hydrochloric acid, will be effected.

If basic acetate of lead is used in excess, the precipitate begins to redissolve; the precipitant should therefore be added very gradually, testing the fluid now and then to ascertain whether the precipitation be complete. I have also observed the precipitate to be soluble in a solution of caustic potash. The lead-compound collected on a filter is to be thoroughly washed, to remove any excess of basic acetate of lead, and a solution of the lead-compound of the colloid acid, to which I shall refer hereafter.

As the lead precipitate appears to be slightly soluble in water, it is difficult to ascertain precisely the period at which the washing may be considered sufficient. I usually continued pouring distilled water into the filter until sulphuretted hydrogen gave but a faint dark colour in the filtrate. The decomposition of the insoluble compound by means of sulphuretted hydrogen is a slow process, and takes some hours before it is complete; and it will be advisable to leave the precipitate in contact with sulphuretted hydrogen overnight: the excess of sulphuretted hydrogen may be expelled by boiling, or by a stream of air, by which latter method the coloration caused by heat is avoided.

The Acid.—The fluid prepared as stated above has a strong acid reaction; exposed to the air for a fortnight, and even for a longer period, it is not altered. When concentrated even by very brisk boiling, it may be considered as undergoing no loss and no decomposition, as shown by the following experiments:—75 cub. centims. of the acid, 5 cub. centims. of which were neutralized by 24·3 cub. centims. of a normal potash solution, were boiled down to 15 cub. centims., then diluted with water to 75 cub. centims., and tested with the normal potash solution; 23·4 cub. centims. of this solution were found necessary to neutralize it. Any decomposition must have been very slight, as the difference between the volumes of the potash solution added before and after the boiling was only of about 1 cub. centim.

As a further proof that the acid is not volatile, I distilled a sample of it in a retort, in the free flame, carrying on the operation until nothing but a dark semifluid mass remained in the retort. The distillate was just faintly acid to the most delicate test paper. In most of my experiments the acid was slightly coloured, and evolved a urinous smell when hot. Under the impression that this odoriferous substance might be a volatile acid, such as those discovered by Städeler*, I was led to examine very carefully the distillate obtained as above. This fluid had a strong smell of urine and the faintest acid reaction. After the fluid was rendered alkaline by baryta, the smell was in no way diminished; so that it could not be owing to an acid; moreover, considering that the colloid acid loses its colour, and apparently in a great measure its odour, after agitation with animal charcoal, we may infer that the odour of urine is owing to a very slight decomposition of the colloid acid which takes place under the influence of heat, and more especially in the presence of free mineral acids.

Returning to the solution of the colloid acid in water: after concentration by heat its colour darkens and it becomes syrupy, with a sharp acid taste, and a slight acrid and astringent after-taste. This taste is perceptible in the solution, even when very dilute. I could never obtain any crystals in this syrup beyond those resulting from inorganic impurities. When dried, the acid assumes the form of a transparent varnish, which, by a temperature of 120° Cent., becomes much darkened. The dried

* *Annal. der Chemie und Pharm.* vol. xxvii. p. 134.

substance is very hygroscopic, and dissolves readily in water (with the exception of some few dark flakes) after exposure for some time at 120° Cent. Alcohol, sp. gr. 827, gives it a dull, opaque appearance, and slightly dissolves it. The dry acid is insoluble in ether, and its solution in diluted alcohol is rendered turbid by ether. When burnt it chars, emitting a pungent smell; the ignition is attended with but a very faint flame, showing that very little hydrogen enters into its composition; nothing but a trace of fixed inorganic residue remains after complete incineration of the acid. The colloid acid was found to have no action on polarized light; it failed to precipitate egg-albumen, but precipitated casein in milk; the precipitate was not redissolved in an excess of the acid, as in the case of acetic acid; although strictly a colloid, it passes through the diaphragm of a dialyzer, but the phenomenon is not near so rapid as in the case of crystalloids. In an alkaline fluid, however, the acid (under the form of a compound) does not find its way so readily through the dialyzer, and its passage is thereby checked in a considerable degree.

The qualitative composition of the colloid acid of urine was obtained by subjecting to analysis its insoluble lead-compound. I found the organic substance to consist only of carbon, hydrogen, and oxygen. I have not yet determined the ultimate quantitative composition of the acid, but have succeeded in showing that it possesses an atomic weight, or combining proportion, thereby proving the acid to be a definite substance; the atomic weight of the acid was determined by the analysis of its insoluble lead-salt and of its baryta-salt. In order to analyze the insoluble lead-salt, a weighed quantity of the compound, dried at 120° Cent., was dissolved in acetic acid, and precipitated by means of sulphuric acid, with the addition of alcohol; the sulphate of lead was collected in a filter, the filter burnt, and the inorganic residue treated with sulphuric acid; the sulphate of lead was finally weighed.

TABLE showing the results obtained from the analysis of the insoluble lead-salt of the Colloid Acid of Urine.

Six samples of the acid.	Weight of lead-compound analyzed.	Weight of protoxide of lead found.	Protoxide of lead in 100 parts of the compound.	Acid in 100 parts of the compound.	
Exp.	gram.	gram.			
I. { A.	0.223	0.146	65.5	34.5	} Average {
I. { B.	0.298	0.2006	67.3	32.7	
II. { A.	0.6575	0.4250	64.6	35.3	} Average {
II. { B.	0.516	0.338	65.5	34.5	
III. { A.	0.3735	0.2360	63.2	36.9	} Average {
III. { B.	0.2835	0.1850	65.3	34.7	
IV.	0.5327	0.3552	66.6	33.4	
V.	0.612	0.5493	66.1	33.9	
VI.	0.7183	0.6828	69.9	31.1	

Average in 100 parts { Oxide of lead..... 66.3
Acid 33.7

Five out of the six analyses were made with the acid slightly coloured, to avoid possible inorganic impurity from the use of animal charcoal. In analysis No. VI. the acid had been treated with animal charcoal, and in this case the percentage of lead was a little higher. It is possible that 33·7 is not the exact percentage of acid in the insoluble lead-compound, although it cannot be far from correct; but when the difficulty of obtaining the lead-precipitate in a pure condition is taken into account, I think it will be admitted that the results of these analyses approach each other closely enough to show that the lead-precipitate of the colloid acid is a definite chemical compound. Adopting the number 33·7 as the percentage of acid, the equivalent weight of the acid and of the compound will be

PbO	111·57	
Acid	56·70	atomic weight of acid.
	168·2	atomic weight of compound.

To prepare the baryta-compound of the colloid acid, I began by decomposing with sulphuric acid a known weight of the lead-salt; and by proceeding as in the case of the analysis of the lead-compound, the amount of the colloid acid present was determined. The acid was entirely washed through the filter along with some free sulphuric acid, and I treated the acid filtrate with carbonate of baryta, the mixture being heated for four or five hours, and filtered the next day; the precipitate on the filter was finally washed with hot distilled water for from four to six days, and even after this lapse of time the washings still contained a trace of baryta. I shall only report two out of several of these analyses, as in the others the deficiency of baryta dissolved was obvious. I have calculated the atomic weight of the acid from the baryta-compound which yielded most baryta, as follows—

Analysis No. I.

		per cent.
Compound of colloid acid and	{ BaO 0·4607 72·2
baryta 0·6382	{ Acid 0·1775 27·8
		100·0

Analysis No. II.

Compound of colloid acid and	{ BaO 0·5950 65·7
baryta 0·9058	{ Acid 0·3108 34·3
		100·0

The atomic weights derived from analysis No. I. are—

BaO	76·39
Acid	29·5
Compound	106·0

If we now compare the atomic weight of the acid in the baryta-compound (29·5) with that in the lead-compound (56·7), it will be readily seen that the relative proportion of these two numbers being very nearly one to two, the lead-compound contains two equivalents of colloid acid ($2 \times 28\cdot3$), and the baryta-salt one equivalent of the acid (28·3); the insoluble lead-compound is therefore an acid salt of the colloid acid. I shall propose the number 28·3 as the atomic weight of the new acid. We are now able to explain why the insoluble lead-salt of the colloid acid is soluble in an alkaline fluid such as potash. Of the two equivalents of colloid acid, one combines with oxide of lead, and the other with potash, forming two soluble neutral salts,

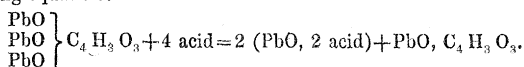


Compounds of the Colloid Acid of Urine.

Lead-salts.—Basic acetate of lead added to the free acid, or solutions of its neutral salts, gives rise to a white precipitate. When a glass rod moistened with a solution of basic acetate of lead is immersed into a moderately strong solution of the free acid, a precipitate forms, which disappears on agitating the fluid; this can be repeated several times before the precipitate becomes permanent. When the fluid no longer turns clear on agitation, the application of heat will dissolve the precipitate, but on the further addition of the precipitant, the hot liquid will soon remain turbid. An excess of basic acetate of lead redissolves the precipitate; this resolution appears to take place more readily when an excess of the precipitant is added to neutral salts of the colloid acid, than when added to the free acid.

After mixing basic acetate of lead with urine, treated as described above, and filtering, I observed that the filtrate still contained much organic matter, although the further addition of the reagent caused no turbidity. I at first naturally thought that this was owing to the presence of another colloid substance in urine; but my surprise was very great when I found that the pure acid obtained by decomposing its insoluble lead-compound could be but partly re-precipitated by means of basic acetate of lead, a comparatively large portion of organic matter remaining dissolved, as shown by evaporating a few drops of the fluid and incinerating the residue, which charred and burnt away, leaving a little oxide of lead on the spatula. Having previously ascertained that the pure basic lead-salt was nearly perfectly insoluble in water, I could not for some time explain the phenomenon. On reflecting upon the fact, it occurred to me that, as the liquor in which the acid had been precipitated appeared to contain some neutral acetate of lead*, possibly this salt had the power of dissolving the precipi-

* The formation of this compound might be considered to have taken place as shown in the following equation:—



pitae; and on mixing some of the precipitate with a solution of neutral acetate of lead, and boiling, I observed a solution of the colloid compound to take place. This experiment, repeated several times with different samples of the insoluble lead-compound of the colloid acid, yielded invariably the same result: although it happened in most cases that the precipitate was not entirely dissolved, it was very obvious that the greater portion of it had disappeared. The phenomenon in question is very interesting, not only because it accounts partly for the fact that basic acetate of lead does not precipitate the whole of the colloid acid of urine, but also because it affords additional proof of the insoluble lead-compound being an acid lead-salt of the colloid acid. A piece of wet blue test-paper is reddened when held over the opening of a test-tube in which the mixture of the precipitate and neutral acetate of lead is being boiled, showing that acetic acid is given off. This would not happen unless there was an acid present to displace the acetic acid from the neutral acetate of lead; and this acid must be the acid lead-salt. There is now no difficulty in accounting for the solution of the acid lead-salt in neutral acetate of lead: one equivalent of the colloid acid combines with one equivalent of lead of the neutral acetate, two equivalents of neutral lead-salt of the colloid acid being formed, $\text{PbO} \cdot 2 (\text{acid}) + \text{PbO} \text{ C}_4 \text{H}_3 \text{O}_3 = 2 (\text{PbO} \cdot \text{acid}) + \text{C}_4 \text{H}_3 \text{O}_3$, while free acetic acid is evolved. On incinerating the acid lead-salt of the colloid acid, it chars and leaves a residue consisting of metallic lead.

By boiling the free acid with a small quantity of hydrated oxide of lead, I have often been surprised at the small proportion of lead dissolved, which is apparently owing to the lead being entirely transformed into the insoluble acid salt. After being boiled with a larger quantity of the oxide and filtered, still acid, a precipitate takes place in the fluid on cooling. This precipitate must be a lead-salt of the acid. I have not determined its quantitative composition. With an excess of hydrated oxide of lead, the colloid acid forms a compound in a great measure insoluble in hot water. After boiling the colloid acid with hydrated oxide of lead, it was observed that a yellowish-green crystalline deposit had formed in the capsule; these crystals, on being burnt, appeared to contain but traces of organic matter. I have not yet been able to determine their nature; but it is difficult to believe them to be a compound of the organic acid with lead, this acid being strictly colloid in all its other properties. When a solution of the salts of the colloid acid is boiled with hydrated oxide of lead, a portion only of the acid is precipitated; so that this method is not available for the extraction of the acid from urine.

When the colloid acid is boiled with peroxide of lead, some lead is dissolved, and the solution becomes neutral, or but very faintly acid. The acid dissolves silver from the carbonate, but it is not possible to neutralize it completely thereby. When boiled with black oxide of copper, some copper is dissolved by the colloid acid.

The Baryta-Salt.—When the colloid acid of urine is boiled with carbo-

nate of baryta, carbonic acid is evolved, the fluid becomes neutral, or very slightly alkaline, and is found to contain baryta. If the insoluble lead-salt of the acid be decomposed with sulphuric acid, and the filtrate from the sulphate of lead boiled with carbonate of baryta, the fluid becomes more decidedly alkaline. The analysis and composition of this baryta-salt has been given above; the solution in a syrupy condition deposits no crystals. The concentrated solution of the baryta-compound behaves as follows with reagents.

Basic acetate of lead :—A bulky precipitate soluble in an excess; the precipitate reappears on addition of dilute nitric acid; the further addition of nitric acid redissolves it.

Neutral acetate of lead :—A slight precipitate.

Nitrate of silver :—A slight precipitate readily soluble in nitric acid.

When the baryta-salt is boiled with carbonate of silver, but a small proportion of the metallic carbonate is decomposed even after long-continued boiling.

Acid nitrate of mercury :—A white precipitate becoming darker after a short time.

Tannic acid :—A slight precipitate.

It should be understood that the more concentrated the solution, the more abundant are the precipitates.

The Lime-Salt.—The lime-salt exhibits the same characteristic reactions as the baryta-salt; it is formed by boiling the free acid with precipitated carbonate of lime. The fluid remained acid after it had been boiled with pounded marble, although some lime was dissolved; concentrated to a certain point, the solution becomes thick and syrupy, but deposits no crystals; ammonia and oxalate of ammonia do not appear to precipitate completely the lime from the solution, but the precipitation is perfect by means of sulphuric acid and alcohol.

The Potash- and Soda-salts.—We may infer from the earthy salts that the potash- and soda-compounds of the colloid acid of urine have a slightly alkaline reaction. There is no difficulty in neutralizing a given volume of the colloid acid with a potash solution, but it is questionable whether a definite chemical compound is thus obtained.

Physiological Relations of the Colloid Acid of Urine.

I have invariably found the colloid acid present in the urine, but its mode of extraction described above is calculated to give us but a very rough insight into the quantity naturally contained in the secretion. After decomposing the lead-precipitate by sulphuretted hydrogen, a process which it must be remembered is a slow one, a given proportion of the fluid may be evaporated to dryness, the residue dried at between 101° and 110° Cent., and its weight ascertained; the result will be obtained somewhat more accurately by determining the ashes of the residue, and subtracting this weight from that of the residue. I have extracted from 8 litres of

urine 4.46 grammes of the colloid acid. This is probably hardly half the quantity contained in that bulk of the secretion. I have some reason to believe that the colloid acid described in this paper is not confined to the urinary fluid, but is found elsewhere in the human body; indeed its secretion by the kidneys shows that it very probably exists in the blood. My experiments on the blood have not yet been carried far enough to enable me to communicate the results obtained from this inquiry.

The functions of the colloid acid of urine while in the blood, assuming that it enters into its composition, must be very important. There can be little doubt that it is intimately connected with the secretion of gastric juice, by displacing the hydrochloric acid of the chloride of sodium in the blood, and transforming the soda into a colloid salt, which, from its colloid nature, would be retained in the blood, while the free hydrochloric acid would pass into the stomach to form gastric juice. I have undertaken an experiment in connexion with this point, which showed that, after dialyzing for five hours a mixture of chloride of sodium and of the colloid acid of urine, the hydrochloric acid had nearly entirely passed through the dialyzer, while rather less than half the amount of the colloid acid had remained on the diaphragm, holding some soda, though a small quantity, in solution; from an accidental omission in my notes, I regret being prevented from giving the details of the experiment.

The free colloid acid being capable to a certain extent of passing through a membrane, its secretion by the kidneys, urine being generally acid, is easily accounted for.

As to the mode of formation of the colloid acid of urine in the human body, we have, so far, no positive knowledge. From its composition and colloid nature, it may probably be derived from some transformation of the colloid non-nitrogenous product of the liver, known as the glucogenic substance.

Neubauer and Vogel's book on urine contains an account of the mode of preparation and characters of four organic acids discovered in this secretion by Städeler, these substances being phenylic, taurylic, damaluric and damolic acid. They are obtained from urine by distillation, and are crystalloids, and therefore can have no relation to the substance I have described in this paper.

When better acquainted with the chemical composition and physiological relations of the colloid acid of urine, I shall be able to give it an appropriate name.